DTIC FILE COPY

(1)

AD _____

EPIDEMIOLOGY AND EPIZOOTIOLOGICAL INVESTIGATIONS OF HEMORRHAGIC FEVER VIRUSES IN THE CENTRAL AFRICAN REPUBLIC

AD-A198 234

Final Report

A. J. Georges and J. L. Durosoir

DTIC
ELECTE
MAR 1 4 1988
S D
H

December 14, 1985

Supported by:

U.S. ARMY MEDICAL RESEARCH AND DVELOPMENT COMMAND
FORT DETRICK, FREDERICK, MARYLAND 21701-5012

CONTRACT NO. DAMD17-84-G-4022

Institut Pasteur
28 Rue du Docteur Roux
5724 Paris, Cedex 15, France

Approved for public release; distribution unlimited

The findings in this report are not to be construed as an official Department of the Army position unless so designated by other authorized documents.

88 3 11 085

UNCLASSIFIED
SECURITY CLASSIFICATION OF THIS PAGE(When Data Entered)

UNCLASSIFIED

AD _____

FINAL REPORT

TITLE

EPIDEMIOLOGY AND EPIZOOTIOLOGICAL INVESTIGATIONS OF HEMORRHAGIC FEVER VIRUSES IN THE CENTRAL ANFRICAN REPUBLIC

TYPE OF REPORT
FINAL REPORT

AUTHOR(s)

A.J. GEORGES and J.L. DUROSOIR

DATE

DECEMBER 14, 1985

(REVISED MARCH 1986)

Supported by

U.S. ARMY MEDICAL RESEARCH AND DEVELOPMENT COMMAND
Fort Detrick,
Frederick, Maryland 21701-5012

Contract No. DAMD 17-84-G-4022 DOD DISTRIBUTION STATEMENT
APPROVED FOR PUBLIC RELEASE: DISTRIBUTION UNLIMITED

DTIC COPY INSPECTED

The findings in this report are not to be construed as an official Department of the Army position unless so designated by other authorized documents

UNCLASSIFIED

For
I ☑
☐
Unannounced. ☐
Justification
By
Distribution/
Availability Codes
Dist | Avail and/or Special
A-1

UNCLASSIFIED
SECURITY CLASSIFICATION OF THIS PAGE(When Data Entered)

UNCLASSIFIED

SECURITY CLASSIFICATION OF THIS PAGE (When Data Entered)

REPORT DOCUMENTATION PAGE	READ INSTRUCTIONS BEFORE COMPLETING FORM
1. REPORT NUMBER / 2. GOVT ACCESSION NO.	3. RECIPIENT'S CATALOG NUMBER
4. TITLE (and Subtitle) EPIDEMIOLOGY AND EPIZOOTIOLOGICAL INVESTIGATIONS OF HEMORRHAGIC FEVER VIRUS IN THE CENTRAL AFRICAN REPUBLIC	5. TYPE OF REPORT & PERIOD COVERED 15 SEP 1984 - 14 SEP 1985 FINAL REPORT
	6. PERFORMING ORG. REPORT NUMBER 0825/IRBA/DIR
7. AUTHOR(s) A.J. GEORGES & J.L. DUROSOIR	8. CONTRACT OR GRANT NUMBER(s) DAMD17-84-G-4022
9. PERFORMING ORGANIZATION NAME AND ADDRESS Institut Pasteur 28 Rue du Docteur Roux 5724 Paris, Cedex 15, France	10. PROGRAM ELEMENT, PROJECT, TASK AREA & WORK UNIT NUMBERS 62770A.3MI62770A871.AP.031
11. CONTROLLING OFFICE NAME AND ADDRESS U.S. ARMY MEDICAL RESEARCH AND DEVELOPMENT COMMAND, ATTN: SGRD-RMI-S, FORT DETRICK, FREDERICK, MD 21701-5012	12. REPORT DATE 12/14/1985 13. NUMBER OF PAGES 16
14. MONITORING AGENCY NAME & ADDRESS(if different from Controlling Office)	15. SECURITY CLASS. (of this report) UNCLASSIFIED 15a. DECLASSIFICATION DOWNGRADING SCHEDULE

16. DISTRIBUTION STATEMENT (of this Report)

APPROVED FOR PUBLIC RELEASE . DISTRIBUTION UNLIMITED

17. DISTRIBUTION STATEMENT (of the abstract entered in Block 20, if different from Report)

18. SUPPLEMENTARY NOTES

NONE

19. KEY WORDS (Continue on reverse side if necessary and identify by block number)

1)HEMORRAGIC FEVERS,2)FILOVIRIDAE,3)CENTRAL-AFRICAN REPUBLIC,
4)EPIDEMIOLOGY,5)EPIZOOTIOLOGICAL INVESTIGATIONS,

20. ABSTRACT (Continue on reverse side if necessary and identify by block number)

EBOLA,MARBURG,CONGO-CRIMEAN-HEMORRAGIC-FEVER,AND RIFT VALLEY FEVER-VIRUS SEEM TO BE ENDEMIC IN THE C.A.R.IN 1984 USAMRIID AND PASTEUR INSTITUTE IN PARIS SET UP A COLLABORATIVE PROGRAM OF RESEARCH WITH INVOLVEMENT OF THE PASTEUR INSTITUTE OF BANGUI LOCATED IN A COUNTRY WERE ANTIBODIES PREVALENCE RATES AGAINST THESE VIRUSES ARE VERY HIGH.
OUT OF 1398 HUMAN SERA COLLECTED OVERALL THE COUNTRY,WE WERE ABLE TO SHOW QUITE A LOW PREVALENCE FOR RVF,CCHF,AND ARENAVIRUSES,AS COMPARED TO A HIGH ONE FOR FILOVIRIDAE.LONG TERM EPIDEMIOLOGICAL STUDIES ARE NEEDED.

DD FORM 1 JAN 73 1473 EDITION OF 1 NOV 65 IS OBSOLETE

UNCLASSIFIED

SECURITY CLASSIFICATION OF THIS PAGE (When Data Entered)

UNCLASSIFIED
SECURITY CLASSIFICATION OF THIS PAGE(When Data Entered)

SUMMARY

Based upon preliminary surveys and/or virus isolations, Ebola, Marburg, Congo-Crimen, haemorrhagic fever and Rift-Valley-Fever virus seem to be endemic in the Central African Republic (CAR). The occurence of these agents poses risk to both the local population, and to travelers or foreigners living in the CAR, who could carry these pathogens out of the country, and infect residents of other parts of the world.

In 1984 US AMRIID and PASTEUR INSTITUTE in PARIS decided to set up a cooperative program of research on Viral haemorrhagic Fevers (VHF), in the CAR. INSTITUTE PASTEUR of BANGUI (IPB) was asked to develop field research and to collect human specimen from numerous villages in an attempt to define the prevalence and distribution of haemorrhagic fever infections in different ecological zones of the country.

Human antibody prevalence rate of VHF has been determined in several areas. A total of 1398 human sera has been obtained. Patients were from the following districts: BANGASSOU (and HAUT MBOMOU): 222; BAMBARI (and OMBELLA MPOKO including BANGUI town): 194; BERBERATI and NOLA area (SANGHA): 292; NDELE area (VAKAGA district): 307; BOSSANGOA (and NANA MAMBERE plus OUHAM PENDE): 383.

Serum samples have been aliquoted, one portion stored at PASTEUR INSTITUTE in BANGUI (IPB) for routine analysis by immunofluorescence assay, and the remaining portion sent to USAMRIID for control and additional analysis by alternative methods.

The sero survey showed a low antibody prevalence against RVF virus, CHF-Congo, and Arenavirus, while interesting data were obtained for FILOVIRIDAE. The sero prevalence for both EBOLA and MARBURG was very high, specially in the NORTHERN DISTRICTS and in the eastern part of the CAR.

These preliminary results document the presence in CAR of virus causing haemorrhagic fevers in other countries of Central Africa, and allow selection of areas for potential long term ecological and epidemiological studies.

Nevertheless these data, remain incomplete at this point, and there is a particular need to continue researchs. The INSTITUTE PASTEUR is most interested in pursuing this continued research in collaboration with USAMRIID.

UNCLASSIFIED
SECURITY CLASSIFICATION OF THIS PAGE(When Data Entered)

UNCLASSIFIED
SECURITY CLASSIFICATION OF THIS PAGE(When Data Entered)

FOREWORD

Since 1979, the IPB research program has concentrated on arbovirus haemorrhagic fever and diarrhoeal diseases. Studies of febrile patients allowed us to identify an infecting arbovirus in about 8% of the patient studies.
In 1980, using FA assay, we started a program of sero surveys of haemorrhagic fevers in the whole country : 2672 human sera have been screened. Based upon these preliminary data and limited virus isolations we were able to show that five hazardous haemorrhagic fever viruses : Ebola, Marburg, Lassa, Congo-Crimean and Rift-Valley-Fever, were endemic in the Central African Republic. These initial successful sero surveys were found interesting by both US AMRIID and IPB and we decided to set up a common research project.

The specific aims of the project were to develop a cooperative program to :
-1) evaluate aims of the potential threat of viral haemorrhagic fever infections in the country by determining antibody prevalence rate in human and animals in several ecological zones.
-2) establish preliminary ecological studies to implicate vertebrates as reservoir and/or vectors, by correlating the antibody prevalence rate in wild peridomestic animals with that in humans.
-3) locate areas for indepth field studies to determine the incidence of subclinical and clinical infections and environmental factors which could influence the maintenance and dissemination of these agents.
-4) evaluate existing serological methods and those currently under developpment such as ELISA or WESTERN BLOTT to establish and control valid fieldable serological assays for the agents.

The initial INSTITUT PASTEUR-US AMRIID haemmorrhagic fever virus sero survey was highly succesful.

It confirmed the Institute's original observations, turned up several interesting and unexpected findings, and established a starting point for more comprehensive and extended studies. Among the six zones we explored, the findings suggest that the VAKAGA district in the North may provide the best opportunity to study the epidemiology of FILOVIRIDAE.

UNCLASSIFIED
SECURITY CLASSIFICATION OF THIS PAGE(When Data Entered)

TABLE CONTENTS

LIST OF APPENDIXES

1 - Scientific publications:

1983

GEORGES A.J., ABDUL-WAHID S.A., MEUNIER D.Y.M., GEORGES M.C., SALUZZO J.F., PETERS C.J., McCORMICK J.B. and GONZALEZ J.P. 1983: Serological equivalence of endemic Zinga Virus and Rift Fever Virus in the Central African Republic. Lancet, June 11: 1338.

GONZALEZ J.P., BUCHMEIER M.C., McCORMICK J.B. and KILEY M.P., 1983: Comparative analysis of several Lassa-Like arenavirus isolated from Africa. In "Negative strand virus" (DHL bishop and RW Compans edit.) Elsevier North Holland, New York.

GONZALEZ J.P., McCORMICK J.B., HERVE J.P., JOHNSON K.M. and GEORGES A.J. 1983: An arenavirus isolated from wild-caught Rodents in the Central African Republic. Intervirology, 19 (2): 105-112.

GONZALEZ J.P., McCORMICK J.B., SALUZZO J.F. et GEORGES A.J. 1983: Les fièvres hémorragiques africaines d'Origine virale en République Centrafricaine. Cah.ORSTOM,Ser.Ent.Méd. et Parasit., XXI, (2): 119-130.

1984

GONZALEZ J.P. 1984: Les arénavirus d'Afrique; essai pour une définition d'un complexe original. Thèse Doc. sér. E.346 Univ. Clermont-Ferrand II. France.

GONZALEZ J.P., BUCHMEIER M.J., McCORMICK J.B., MITCHELL S.W., ELLIOTT L.H. and KILEY M.P., 1984: Comparative analysis of severalLassa-like arenavirus isolates from Africa. In "Negative Strand Virus" DHL Bishop and R.W. Compans eds. Elsevier/North Holland, New York. Acad.Press, Inc: 201-208.

GONZALEZ J.P., McCORMICK J.B., BAUDON D., GAUTUN J.P., MEUNIER D.Y., DOURNON E., and GEORGES A.J., 1984: Serological evidence for Hantaan-Related Virus in Africa. Lancet., ii, Nov. 1984.

GONZALEZ J.P., McCORMICK J.B., GEORGES A.J. and KILEY M.P., 1984: Mobala Virus: Biological and Physico-chemicals properties of a new arenavirus isolated in the Central African Republic.

Ann.Virol.Inst.Pasteur, 135 E: 145-158.

1985

GEORGES A.J., GONZALEZ J.P., ABDOUL-WAHID S., SALUZZO J.F., MEUNIER D.M.Y. and McCORMICK J.B. 1985: Antibodies to Lassa and Lassa-like viruses in man and mammals in the Central African Republic. Trans.R.Soc.Trop.Med.Hyg., 79:78-79.

MEUNIER D.Y., McCOMICK J.B., GEORGES A.J., GEORGES M.C. and GONZALEZ J.P. 1985: Comparaison of Lassa,Mobala and Ippy Virus Reaction by Immunofluorescence test. Lancet: 873-874

GONZALEZ J.P. 1985: Les arenavirus d'Afrique. Un nouveau paradigme d'évolution. Bull.Inst.Pasteur (in press)

GONZALEZ J.P., McCORMICK J.B. and KILEY M.P. 1985: Genetic variation among Lassa and Lassa related arenaviruses from different African Origins. Virology (in press)

2 - SCientific communications, Reports and Documents

1983

GEORGES A.J., GONZALEZ J.P., McCORMICK J.B., MEUNIER D.M.Y., 1983: Epidémiologie des Fièvres Hémorragiques Africaines d'origine virale. In Rapport sur le fonctionnement de l'Institut Pasteur: 24-40.

GONZALEZ J.P. (Mars 1983): Prélèvement et traitement des produits biologiques issus de malades suspects de Fièvre Hémorragique et destinés à l'analyse de laboratoire. (Doc. dactyl., CDC), pp. 2.

GONZALEZ J.P., BUCHMEIER M.J., McCORMICK J.B., MITCHELL S.H., HELIOTT L.E. and KILEY M.P. 1983: Comparative analysis of several Lassa-like arenavirus isolates from Africa. 15ème Réunion de l'Amer.Soc.Hyg.Trop.Med.,Ken.Univ.,USA.

1984

GONZALEZ J.P., GEORGES A.J., McCORMICK J.B. and KILEY M.P. 1984: Biological and Physico-Chemical Charateristics of several Lassa and Lassa related African arenaviruses. Sixth International Congress of Virology, Sendai, Japan: p. 27, 17. Abstract: 273, T

1985

GONZALEZ J.P., GEORGES A.J., KILEY M.P., MEUNIER D.M.Y., PETERS C.J. and McCORMICK J.B. 1985: Evolutionary biology of a Lassa Complex. Meeting an Arenaviruses. H.Pette Institute. Hamburg, Sptember.

GONZALEZ J.P., KILEY M.P., MEUNIER D.M.Y., GEORGES A.J. and McCORMICK J.B. 1985: Evolutionary biology of some arenaviruses from Africa. The biology of Negative Strand Viruses. Cambridge U.K. September.

JOHNSON E.D., PETERS C.J., GONZALEZ J.P., MEUNIER D.Y., GEORGES A.J. 1985: Ebola Hemorrhagic Fever (EHF): Preliminary Seroepidemiological Investigation in the Central African Republic. Institute Pasteur, Bangui, Central African Republic. USAMRIID, Fort Detrick, Frederick, Maryland 21701-5011, USA: 10-12, Rabat

MEUNIER D.M., GONZALEZ J.P., PETERS C.J., JOHNSON E. et GEORGES A.J. 1985: Surveillance épidémiologique des Filoviridae en RCA. Institut Pasteur, B.P. 923, BANGUI - République Centrafricaine - USARMIID, FORTDETRICK USA. Rabat, Maroc.

GEORGES A.J.,GONZALEZ J.P.,McCORMICK J.B. and MEUNIER D.M.Y.-1984, Epidemiologie des Fiévres Hémorragiques africaines d'origine virale . Rapport bisannuel de l'Institut Pasteur de Bangui 1982-83.

REPORT

Between October 1984 and July 1985, we were able to collect 1398 human sera from 6 districts of the CAR. All the specimens were screened double blind at 1/16 dilution on CRELM slides and the positive tited on monovalent antigen spots. This screening has been performed in BANGUI as well as in FREDERICK .The IFA data on CCHF, Rift and Lassa are unimpressive, while data concerning Filoviridae are really very interesting.

Methods :
Five different areas have been studied :
1 : BANGASSOU and villages around this main town located in the district of HAUT MBOMOU. 222 samples were collected. In this area, in 1979 we observed 2 persons with fluorescent MARBURG antibodies (1).

2 : BAMBARI and OMBELLA MPOKO district including BANGUI, capital of the country : 194 patients were sampled.

3 : BERBERATI and NOLA area (SANGHA) : 292 patients bled.

4 : BOSSANGOA and NANA MANBERE : 293 sera collected.

5 : VAKAGA district : 307 people studied.

In each village 5 to 10 houses, were selected. All individuals between 10 and 50 years of age were identified and sampled. Lists of persons with family name, first name, and approximate age, have been established for further vertical studies.
In 1985 a second trip only in the VAKAGA district allowed us to check some patients. In some areas wild peridomestic and domestic animals have been bled and some of the rodents organs have been treated for viral isolation. Serum samples have been aliquoted and sent to USAMRIID in liquid nitrogen as previously asked in the contract.

Results:
Between 9% and 37% of the whole population are positive for 1 or more of the viral antigen. In fact the prevalence of antibodies is different whether we consider each family of virus.
BUNYAVIRIDAE AND PHLEBOVIRUS (RVF):
Up to now, serosurveys have shown a low prevalence of the [illegible]rus : 0.4% for the whole country. Nevertheless in several areas antibody prevalence rates demonstrate RVF virus circulation. Sera found to be positive for FA, have been controlled using neutralisation.
Complete results are given in table 1:

Table 1 :
Rift-Valley-fever virus serosurvey :

DATE OF SAMPLING	ORIGIN	TOTAL	POS	% POS
JUN 84	PAOUA	96	0	0
JUN 84	BANGUI	101	1	1
JAN 85	BALEMBE	31	0	0
JAN 85	BOUAR	112	2	1.8%
JAN 85	DIKA	75	0	0
JAN 85	DONGO BODAMA	59	0	0
JAN 85	NDONGUE	10	0	0
FEB 85	ZEMIO	140	0	0
FEB 85	BAMBOUTI	82	0	0
TOTAL		706	3	0.4%

In 1984,we isolated 3 new Rift-Valley-fever virus strains in CAR.
2) Nairoviruses : CHF Congo virus.
The sero survey has shown a low prevalence of the CHF Congo virus in the CAR : 1.7% .
The complete results are given in table 2. We must note that all the positive sera were from the same area in the North-West of the CAR, including two important towns : Bouar and Boguila.

Table 2:
CCHF virus serosurvey :

Date of Samples		Geographical origin	N° Tested	N° Pos	% Positive
June	1984	PAOUA	96	1	1
June	1984	BANGUI	101	0	0
January	1985	BALEMBE	31	0	0
January	1985	BOUAR	112	4	3.6
January	1985	DIKA	75	4	5.3
January	1985	DONGO BODAMA	59	3	5.1
January	1985	NDONGUE	10	0	0
February	1985	ZEMIO	140	0	0
February	1985	BAMBOUTI	82	0	0

One strain of CCHF virus was isolated from a wild rodent Mastomys sp, caught in the North-West of the CAR, near the town of Boheng.

-3) Arenaviridae :
All the surveys have shown a very low prevalence for Lassa virus antibodies (0.8%). The complete results are given in table 3.

Table 3 :
Distribution of Fluorescent antibodies against Lassa, Mopeia, and Mobala viruses.

Location	Total sera tested	Positive sera		
		Lassa V.	Mopeia V.	Mobala V.
Bangassou	22	0	0	0
Botambi	53	0	0	0
Bouar	229	5	1	0
Bouboui	127	0	0	4
Bozo	40	0	0	0
Gomoka	78	0	0	3
Zemio	166	0	0	0

4) Filoviridae :
13% of the CAR samples were found to contain Filoviridae virus specific antibody when screened at a 1 to 16 dilution in an indirect immunoflucrescent antibody assay using polyvalent CRELM slides.
All the positive specimens were subsequently titrated on monospecific slides with Ebola, Marburg antigens. The overall antibody prevalence was quite similar to those reported from other countries of the central Africa : Cameroon (1), Zaire (2,3), and Sudan (4,5) ; but higher than that in Gabon (6).
The lowest antibody prevalence was found in the forested Sangha district which is located in the South of the country : 9.9%.
In drier districts such as Ombella-M'Poko, we found a prevalence around 16%.
In the Vakaga district, the prevalence was also around 16%. These findings dispel the idea that human Filovirus infections occur predominently in moist tropical forest or are associated with particular climatic zones.
Recently, antibodies against Marburg virus have been found in some villages of the district of Vakaga. The specimen found to be positive had been previously collected in children between ten and fifteen years old. In March 1985, we set up a sero survey in Chad in the North of the Vakaga district.In this region, the antibodies against Filoviridae were found to be very high,more than 50%.
We give below in two tables (4,5) the results of 1398 FA tests.

In 1984,a first sero survey showed a high prevalence for EBOLA & MARBURB VIRUS in the CAR:30.8%.
Complete results are listed in table 4.

Table 4:

DATE	ORIGIN	TOTAL	MARBURG	EBOLA (Z)	EBOLA (S)
JUN 84	PAOUA	96	2 / 2.1%	4 / 4. 2 %	1 1%
JUN 84	BANGUI	101	0 / 0 %	3 / 3. 0 %	0 0%
JAN 85	BALEMBE	31	1 / 3.2%	2 / 6. 5 %	1 3.2%
JAN 85	BOUAR	112	1 / 0.9%	9 / 8. 0 %	7 6.3%
JAN 85	DIKA	75	5 / 6.7%	9 /12. 0 %	8 10.7%
JAN 85	DONGO BODAM	59	1 / 1.7%	2 / 3. 4 %	1 1.7%
JAN 85	NDONGUE	10	0 / 0.0%	0 / 0. 0 %	0 0.0%
FEB 85	ZEMIO	140	0 / 0.0%	65 /46. 4 %	0 0.0%
FEB 85	BAMBOUTI	82	0 / 0.0%	50 /61. 0 %	0 0.0%
	TOTAL	706	10 / 1.4%	144/ 20. 4 %	18 2.5%

In the beginnig of 1985, a second sero survey was undertaken in 3 different areas : SANGHA (Dense forest), OMBELLA MPOKO (Wet savannah), VAKAGA (Pseudo steppe) . Thirteen per cent of these samples (93/692), were found to contain filovirus specific antibodies when screened at a 1/16 dilution, using an indirect immunofluorescent antibody assay. Complete results are listed below, in table 5.

Table 5 : Distribution of FILOVIRUS activity in 3 districts of the CAR (1985):

DISTRICT	VILLAGE	ANTIBODY PREVALENCE (FA) POS.	TOTAL TEST.	%
SANGHA	LIDJOMBO	17	163	10.4%
	BAYANGA	10	97	10.3%
	BABINGO	2	32	6.3%
OMBELLA MPO.	BOZO	15	93	16.1%
VAKAGA	TOUMOU	29	128	22.6%
	AMARDJEDI	3	80	3.8%
	SIKIKEDE	17	99	17.2%
		93	692	13.0%

The overall activity was quite similar to those reported from other parts of central Africa : CAMEROON (4), ZAIRE (5,6), SUDAN (7,8). Nevertheless, this activity seems lower than in GABON (9), but we must note that the studies in that country were undertaken on quite a small number of sera.
Data obtained dispel the idea that human filovirus infection occur essentially in moist tropical forest. In the CAR, and perticularly in the VAKAGA district, the antibody rate is about 5 times that found in the arid scrub savannah sample in CAMEROON or in GABON. They merit being compared to those obtained in KENYA .
The VAKAGA findings are particularly surprising since the populations are of the same tribe (They were living in the same village 10 years ago!)

The distribution of end point IFA titers is also interesting but difficult to understand : monospecific EB.sudan are low titered, double positives have similar titer for both EB.Sudan & Zaire though a little bit higher. The possibility of less pathogenic strains is consistent with the somewhat high antibody prevalence as compared to apparent lack of clinical disease. These observations must be compared to those recently obtained in CHAD (Dr.GEORGES : unpublished personnal data).
MARBURG results obtained by USAMRIID also seem significant, and there is a need for complementary studies.

Discussion:

More detailed study of PHLEBOVIRUS and FILOVIRUS in the CAR is warranted.A number of problems responsible for limitations of previous studies have been overcome. The cooperative programm of research set up by USAMRIID and PASTEUR INSTITUTE was successful and allowed us to establish a productive study area.
There are many advantages to studying hemorrhagic fever virus in both OMBELLA MPOKO (RVF), and VAKAGA (EBOLA & MARBURG) districts. Several factors lend credibility to undertaking longitudinal studies in these districts.

CONCLUSIONS:
The striking focality of FILOVIRUS activity in the VAKAGA DISTRICT of the CAR represents an exciting finding. It seems interesting to follow the people showing antibodies.

Proposals for continuing the already successful collaboration between USAMRIID and IPB, to study hemorragic fever viruses in the CAR merit being prepared and discussed.
In the VAKAGA district,or in other area with moderate but real filovirus activity,it is important to select and then to follow up a well defined study population.Demographic information must be collected in each village.Fifty to one hundred antibody negative families with presumably similar risk will be choosen to participate in a longitudinal seroepidemiological study.Selected people must be bled at least two or three times each year.Incentive drugs or if necessary and possible,a dispensary will be given to selected villages.
Virus animal interaction merit in being studied in the areas and in the species(peridomestic or wild,or both)which seem to be involved in the biology of FILOVIRUSES.
A research budget including personnel and research support must be accepted before starting this second part of the prosed research program:the global amount could be around 55,000 US Dollars for the first year.A complete evaluation could necessitate at least 2 or 3 years.

LITERATURE CITED

1-SALUZZO & al:Mise en evidence d'anticorps vis à vis du virus Marburg parmi les populations humaines du Sud Est de la R.C.A.
C.R. ACAD.SC.PARIS.1981,292,1,pp.29,31

2-GEORGES & al:Arboviroses en Centrafrique;incidence et aspects diagnostiques chez l'homme.
MED.TROP.,1980,5,561-568

3-GONZALEZ & al:Les fièvres hémorragiques africaines d'origine virale:contribution à leur étude en R.C.A.
CAH.MICROB.PARASITOL.ENTOM.MED.ORSTOM,1983,2,pp.119-130

'RNEE & al:Ebola virus infection in man:a serological and epidemiological survey in the CAMEROON .
AMER.J.TROP.MED. HYG.1983;32(6),1465-1466

5-HEYMANN & al:Ebola hemorragic fever:Tandala , Zaire 1977-1978?
J.INF.DIS.1980,142(3),372-376;

6-JOHNSON & al:Personal communication

7-MEEGAN & al:Personal communication

8-JOHNSON & WILLIAMS :unpublished observations

9-IVANOFF & al:Hemorragic fever in GABON.I.Incidence of Lassa ,Ebola and Marburg virus in Haut Ogoué.
TRAN.ROY.SOC.TROP.MED.HYG.1982,76(6),719-720.

10-JOHNSON & al:Antibodies against hemorragic fever viruses in Kenya populations .
TRAN.ROY.SOC.TROP.MED.HYG.1983,77(5),731-733.